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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/668,846	09/23/2003	Graham Smith	GP30201V	4957

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EXAMINER	
LOCKARD, JON MCCLELLAND	
ART UNIT	PAPER NUMBER
1647	

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09/05/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/668,846	SMITH ET AL.	
	Examiner	Art Unit	
	Jon M. Lockard	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) *1,2 and 5-8* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3 and 4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-8* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/523,860.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/25/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, and/or Claims

1. The Amendment filed 25 June 2007 has been received and entered in full. Claims 1-8 are pending and claims 1, 2, and 5-8 stand withdrawn, from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, Therefore, claims 3-4 are under consideration and the subject of this Office action.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Objections and/or Rejections

3. The objections to the Specification as set forth at pg 3 of the previous Office action (mailed 23 February 2007) are withdrawn in view of the amended Specification (filed 25 June 2007).

Maintained Objections and/or Rejections

Claim Rejections - 35 USC § 101 and 35 USC § 112, 1st Paragraph

4. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

> The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 3 and 4 remain rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility, or a well established utility. Novel biological molecules lack an established utility and must undergo extensive experimentation to determine an appropriate specific and substantial utility. The basis for this rejection is set forth for at pg 4-9 of the previous Office Action (mailed 23 February 2007).

6. The instant application discloses an isolated VANILREP4 polypeptide with an amino acid sequence set forth as SEQ ID NO:2. The specification asserts that the VANILREP4 polypeptides of the instant invention are believed to be members of the ion channel family of polypeptides, having homology and/or structural similarity with the rat vanilloid receptor VR1 (See pg 2, lines 23-25; pg 5, lines 9-11). The Specification discloses that the expression of VR-4 mRNA was highest in kidney, and generally higher in many peripheral tissues (e.g., liver, pancreas, placenta, and prostate) than in the CNS, where the highest levels were observed in the corpus callosum, hippocampus, spinal cord, and pituitary gland (See Example 1, pg 23 lines 1-24). Moreover, Example 2 of the Specification also discloses that HEK293 cells transiently expressing hVR4 were activated by PMA (12-myristate 13-acetate) and 4αPDD (4α-phorbol-12,13-didecanoate) (See pg 23-24). There is no well-established utility for a specific VANILREP4 nucleic acid or amino acid sequence, and the specification fails to disclose a specific and substantial utility for the claimed invention. The instant application does not disclose a specific biological role for the claimed VANILREP4 protein or the nucleic acid that encodes it, or its significance to a particular disease, disorder, or physiological process which one would manipulate for a desired physiological or clinical effect.

7. Applicant's arguments (filed 25 June 2007) as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

8. Applicant argues at pg 6 of the response that, contrary to the Examiner's assertion, the specification lists several diseases for which the claimed polypeptides have substantial and credible utility (see pg 1, line 32 through pg 2, line 6).

9. Applicant's arguments (filed 25 June 2007) have been fully considered but are not persuasive for the following reasons. It is noted that Applicant has not provided any evidence or reference of record to substantiate the allegation that the claimed VANILREP4 protein set forth as SEQ ID NO:2 is involved in any disease or disorder, or that molecules that interact with it or modulate its activity can be used to treat any disease or disorder.

> It must be emphasized that arguments of counsel alone cannot take the place of evidence in the record once an examiner has advanced a reasonable basis for questioning the disclosure. See *In re Budnick*, 537 F.2d at 538, 190 USPQ at 424; *In re Schulze*, 346 F.2d 600, 145 USPQ 716 (CCPA 1965); *In re Cole*, 326 F.2d 769, 140 USPQ 230 (CCPA 1964). For example, in a case where the record consisted substantially of arguments and opinions of applicant's attorney, the court indicated that factual affidavits could have provided important evidence on the issue of enablement. See *In re Knowlton*, 500 F.2d at 572, 183 USPQ at 37; *In re Wiseman*, 596 F.2d 1019, 201 USPQ 658 (CCPA 1979).

Moreover, there is no evidence of record to support a conclusion that the VANILREP4 polypeptides of the instant invention are associated in any way with the plurality of causally unrelated disorders that are listed on pages 1-2 of the instant specification, including various forms of pain, neuropathies, nerve injury, ischemia, neurodegeneration, stroke, incontinence, inflammatory disorders, irritable bowel syndrome, diabetes, or obesity. Until some actual and

specific activity or significance can be attributed to the protein identified in the specification as VANILREP4 (SEQ ID NO:2) or the polynucleotide encoding it (SEQ ID NO:1), the claimed invention is incomplete. In the absence of a knowledge of the biological significance of this protein, there is no immediately obvious patentable use for it. Furthermore, to employ a protein of the instant invention in the identification of substances which stimulate or inhibit its activity is clearly to use it as the object of further research, which has been determined by the courts to be a utility, which alone, does not support patentability.

10. Applicant argues at pg 6 of the response that the specification directs the skilled artisan to certain tissue types that contain mRNA encoding the VANILREP protein of SEQ ID NO:2, and provides methods for detecting agonists and antagonists to VANILREP4 polypeptides as well as providing two examples of agonists to this receptor.

11. Applicant's arguments (filed 25 June 2007) have been fully considered but are not persuasive for the following reasons. While the Specification discloses that the expression of VR-4 mRNA was highest in kidney, and generally higher in many peripheral tissues (e.g., liver, pancreas, placenta, and prostate) than in the CNS, where the highest levels were observed in the corpus callosum, hippocampus, spinal cord, and pituitary gland (See Example 1, pg 23 lines 1-24), mere expression pattern in various tissues is not accepted by those of skill in the art as being predictive of function. The instant application does not disclose a specific biological role for the claimed VANILREP4 protein or the nucleic acid that encodes it, or its significance to a particular disease, disorder, or physiological process which one would manipulate for a desired physiological or clinical effect. Without any biological activity or link to a disease, further

research would be required to determine the properties of the claimed VANILREP4 of SEQ ID NO:2 or to identify a disease that can be treated or diagnosed with the claimed molecules, which is insufficient to meet the requirement of 35 USC § 101.

12. The art teaches that members of the vanilloid receptor family are activated by a diverse range of stimuli, including heat, protons, lipids, phorbols, phosphorylation, changes in extracellular osmolarity and/or pressure, and depletion of Ca^{2+} stores, and that understanding how these proteins are assembled, activated, and regulated is a prerequisite for determining the probable role of these receptors *in vivo* (Gunthorpe et al. (2002). TRENDS in Pharmacological Sciences; cited in the previous Office action). Furthermore, while the Specification of the Instant Application discloses that the VANILREP4 polypeptide of SEQ ID NO:2 displays some sequence and structural homology to the rat vanilloid receptor VR1, it is noted that the results presented in Example 2 demonstrate that, in contrast to hVR1, hVR4 is not activated by RTX or capsaicin, which are known agonists of the VR1 vanilloid receptor. Moreover, while the specification discloses that both PMA and 4αPDD activate the hVR4 receptor in HEK293 cells expressing recombinant hVR4, the specification as filed fails to disclose the physiological consequence of that activation or any beneficial effect from said activation, and there is no evidence of record that this *in vitro* activity is predictive of any particular *in vivo* activity. In summary, the specification fails to establish a nexus between the observed hVR4 activity in a recombinant cell line and a physiologically relevant process which one would wish to manipulate (i.e., via administration of an agonist or antagonist) to achieve a beneficial effect in an individual with pain, neuropathies, nerve injury, ischemia, neurodegeneration, stroke, incontinence, inflammatory disorders, irritable bowel syndrome, diabetes, or obesity.

13. Although the homology of the vanilloid receptor family of ion channels, especially in the 6 transmembrane domain regions, allows identification of such as vanilloid receptors, such is not predictive of function. Furthermore, whereas one could readily employ the putative VANILREP4 protein of the instant invention in an assay to identify modulators thereof, the information obtained from such assays would be of little use until one discovers the identity of those physiological processes mediated by that putative VANILREP4 protein. Because the instant specification has failed to identify a physiological process which has been shown to be influenced by the activation or inhibition of the putative VANILREP4 protein of the instant invention, an artisan would have no way of predicting what effects the administration of that modulator to an organism would have. If one cannot predict the effects that the administration of a modulator of the VANILREP4 protein of the instant invention is going to have on an organism, then it is unclear as to what practical or real world benefit is derived by the public from the identification of that modulator.

14. It is possible that, after further characterization, the putative VANILREP4 protein may be found to have a specific and substantial credible utility. This further characterization, however, is part of the act of invention, and until it has been undertaken, Applicant's claimed invention is incomplete. The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sup. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts

when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. §101, which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility. The court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion."

In the Instant case, the instant specification leaves it to the practitioner to discover the identity of a disease or disorder in which the claimed VANILREP4 protein of the instant invention is associated, or which mutated or aberrantly expressed; and then to discover the nature of that aberrant expression (i.e., overexpression or underexpression). The evidence of mere identification as a vanilloid receptor based on sequence homology and expression of the mRNA in various tissues is not tantamount to a showing of a role of the claimed polypeptide of SEQ ID NO:2 in the diagnosis of a disease/disorder, or that compounds that modulate its activity are useful in the treatment of a disease or disorder. Therefore, the claimed polynucleotide or the protein encoded thereby cannot be used in a diagnostic or therapeutic capacity without the need for a substantial inventive contribution. Such additional experimentation, if needed to identify a specific utility for an invention, is precluded by the court.

15. Applicant argues at pg 6 of the response that "the PTO has the initial burden of challenging a patent applicant's presumptively correct assertion of utility" add asserts that the

Examiner has not fulfilled his burden under the law to challenge the Applicant's presumptively correct asserted utility.

16. Applicant's arguments (filed 25 June 2007) have been fully considered but are not persuasive for the following reasons. In the previous Office Action of 23 February 2007, the Examiner made a *prima facie* showing that the claimed invention lacks utility and provided sufficient evidentiary basis for factual assumptions relied upon in establishing the *prima facie* showing (see pg 4-9). The truth, or credibility, of the assertion of utility has not been questioned. Rather, the rejection sets forth that the assertion of utility is not specific or substantial. Essentially, Applicant has not provided evidence to demonstrate that the claimed polypeptide of the instant application is supported by a specific and asserted utility or a well-established utility. It is noted that M.P.E.P. 2107.01 states:

> Deficiencies under the "useful invention" requirement of 35 U.S.C. 101 will arise in one of two forms. The first is where it is not apparent why the invention is "useful." This can occur when an applicant fails to identify any specific and substantial utility for the invention **or fails to disclose enough information about the invention to make its usefulness immediately apparent to those familiar with the technological field of the invention**. Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (1966); In re Ziegler, 992 F.2d 1197, 26 USPQ2d 1600 (Fed. Cir. 1993). The second type of deficiency arises in the rare instance where an assertion of specific and substantial utility for the invention made by an applicant is not credible (**Emphasis added**).

In the instant case, the instant specification leaves it to the skilled artisan to 1) identify a specific biological role for the VANILREP4 polypeptide or its significance to a particular disease, disorder, or physiological process which one would want to manipulate for a desired physiological or clinical effect; and 2) determine whether compounds that inhibit the VANILREP4 polypeptide could be used in methods of treatment, or whether compounds that potentiate/promote the VANILREP4 polypeptide could be used in treatment methods.

17. The Examiner has fully considered all evidence of record and has responded to each substantive element of Applicant's response.

Claim Rejections - 35 USC § 112, 1st Paragraph

18. Claims 3 and 4 also remain rejected under 35 U.S.C. 112, first paragraph for reasons set forth at pg 9 of the previous Office Action (mailed 23 February 2007). Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Summary

19. No claim is allowed.

20. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jon M. Lockard** whose telephone number is **(571) 272-2717**. The examiner can normally be reached on Monday through Friday, 7:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Manjunath N. Rao**, can be reached on **(571) 272-0939**.

The fax number for the organization where this application or proceeding is assigned is **571-273-8300**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see **http://pair-direct.uspto.gov**. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

Jon M. Lockard, Ph.D.
August 28, 2007

CHRISTINE J. SAOUD
PRIMARY EXAMINER